

AMENDMENTS TO THE SPECIFICATION

In the Application:

Please replace the Sequence Listing on file with replacement pages 1-92, attached hereto.

In the Specification:

Please amend the Specification as follows. Paragraph numbers correspond to the paragraph numbering set forth in published PCT application PCT/US03/24488.

Please replace paragraph [00013] beginning on page 5 with the following amended paragraph:

[00013] The allatostatins are an important group of insect neurohormones controlling diverse functions including the synthesis of juvenile hormones known to play a central role in metamorphosis and reproduction in various insect species. The very first *Drosophila* allatostatin, Ser-Arg-Pro-Tyr-Ser-Phe-Gly-Leu-NH₂ (i. e., drostatin-3) (SEQ ID NO: 165), was isolated from *Drosophila* head extracts (Birgul et al. , EMBO J. , 1999,18, 5892-5900). Recently, a *Drosophila* allatostatin preprohormone gene has been cloned which encodes four *Drosophila* allatostatins: Val-Glu-Arg-Tyr-Ala-Phe-Gly-Leu-NH₂ (drostatin-1) (SEQ ID NO: 163), Leu- Pro-Val-Tyr-Asn-Phe-Gly-Leu-NH₂ (drostatin-2) (SEQ ID NO: 164), Ser-Arg-Pro- Tyr-Ser-Phe-Gly-Leu-NH₂ (drostatin-3) (SEQ ID NO: 165), and Thr-Thr-Arg-Pro- Gln-Pro-Phe-Asn-Phe-Gly-Leu-NH₂ (drostatin-4) (SEQ ID NO: 166) (Lenz et al., Biochem. Biophys. Res. Comm., 2000,273, 1126-1131). The first *Drosophila* allatostatin receptor was cloned by Birgul et al. and was shown to be functionally activated by drostatin-3 via Gi/Go pathways (Birgul et al. , EMBO J. 1999,18, 5892-5900). A second putative *Drosophila* allatostatin receptor (i. e., DARII) has been recently cloned (Lenz et al. , Biochem. Biophys. Res. Comm., 2000,273, 571- 577). The DARII receptor cDNA (Accession No. AF253526) codes for a protein that is strongly related to the first *Drosophila* allatostatin receptor. Recently, functional activation of DARII by allatostatins have been shown by us (Larsen, et al. , Biochem. Biophys. Res. Comm. , 2001,286, 895-901) and others (Lenz, et al., Biochem. Biophys. Res. Comm. , 2001, 286, 1117-1122). Recently, a *Drosophila* allatostatin type C preprohormone gene has been cloned which encodes a

Drosophila allatostatin type C preprohormone gene has been cloned which encodes a Drosophila allatostatin-C : Gln-Val-Arg-Tyr-Gln-Cys-Tyr-Phe-Asn-Pro-Ile-Ser- Cys-Phe-OH (SEQ ID NO: 73) (Williamson et al. , Biochem. Biophys. Res. Comm. , 2001,282, 124-130). The mature peptide should have a pGlu at the N-terminus, formed as a result of the N-terminal Gln cyclization, to yield: pGlu-Val-Arg-Tyr-Gln-Cys-Tyr-Phe- Asn-Pro-Ile-Ser-Cys-Phe-OH (~~SEQ ID NO: 183~~) (SEQ ID NO:88), and a disulfide bridge between Cys6 and Cys13, similar to the Manduca sexta type C allatostatin, pGlu-Val-Arg- Phe-Gln-Cys-Tyr-Phe-Asn-Pro-Ile-Ser-Cys-Phe-OH (~~SEQ ID NO: 182~~). (SEQ ID NO:232), which differs only at position 4 (Phe4 vs Tyr4) (Kramer et al., Proc. Natl. Acad. Sci. USA, 1991,88, 9458-9462). Nichols at al., showed potent and prolonged inhibition of muscle contraction of the Drosophila allatostatin-C and named it a flatline (FLT) peptide (Nichols et al. Peptides, 2002,23, 787-794). To our knowledge, to date no receptors for insect allatostatin type-C have been identified.

Please replace paragraph [00014] beginning on page 6 with the following amended paragraph:

[00014] The sulfakinins are a family of insect Tyr-sulfated neuropeptides. They show sequence and functional (myotropic effects, stimulation of digestive enzyme release) similarity to the vertebrate peptides gastrin and cholecystokinin. A gene encoding two sulfakinins (also called drosulfal inins), DSKI [Phe-Asp-Asp- Tyr (S03H)-Gly-His-Met-Arg-Phe-amide] (SEQ ID NO: 160) and DSKII [Gly-Gly- Asp-Asp-Gln-Phe-Asp-Asp-Tyr (S03H)-Gly-His-Met-Arg-Phe-amide] (SEQ ID NO: 161), has been identified in Drosophila melanogaster (Nichols, Mol. Cell Neuroscience, 1992,3, 342-347; Nichols et al. , J. Biol. Chem., 1988, 263,12167- 12170). The C-terminal heptapeptide sequence, Asp-Tyr (S03H)-Gly-His-Met- Arg-Phe-amide (SEQ ID NO: 162), is identical in all sulfakinins identified so far from insects that are widely separated in evolutionary terms. The conservation of the heptapeptide sequence, including the presence of the sulfated Tyr residue, in widely divergent insect taxa presumably reflects functional significance of this myotropic"active core" (Nachman & Holman, in Insect Neuropeptides: Chemistry, Biology and Action, Menu, Kelly & Massler, Eds. , American Chemical Society, Washington, D.

C. , 1991, pp. 194-214). Recently, we identified the Drosophila orphan receptor (DmGPCR9) as a drosulfakinin receptor (named DSK-R1) and matched it with its activating peptide, a MetSOLeu modified drosulfakinin-1, Asp- Tyr (S03H)-Gly-His-Leu-Arg-Phe-amide (~~SEQ ID NO: 157~~) (SEQ ID NO:230) (Kubiak et al., Biochem. Biophys. Res. Comm. , 2002,291, 313-320). The new de-orphaned Drosophila GPCRs include receptors for PRXamide peptides, CCAP, corazonin, and AKH (Park et al., Proc. Natl. Acad. Sci. USA, 2002,99, 11423-11428; Cazzamali et al., Biochem. Biophys. Res. Comm., 2002,298, 31-36); leukokinin (Radford et. al. , J. Biol. Chem. 2002,277, 38810-38817) ; Drostatin-C (Kreienkamp et al. , J. Biol. Chem, 10.1074/jbc. M206931200 (published online 6 August 2002)) ; FMRFamide (Cazzamali et al. Proc. Natl. Acad. Sci. USA, 2002, 99,12073-12078) ; and neuropeptide F (Mertens, et al., Biochem. Biophys. Res. Comm. , 2002,297, 1140-1148).

Please replace paragraph [000244] beginning on page 79, with the following amended paragraph:

[000244]

Table 6. DNA Sequencing Primers

DmG PCR	5' Primer	3' Primer	Internal Primers	
			Sense	Antisense
1	VGS28-gtagcc gccATGGCCAAC TTAAGCTGGCTG AGCAC (SEQ ID NO:184) (<u>SEQ ID NO:228</u>)	VGS29-gtaTCA GTTGATTTCGCCT CCCCAGCTCT (SEQ ID NO:185) (<u>SEQ ID NO:229</u>)	VGS49-TGCAGC ATCTACATATCC ACGCTGA (SEQ ID NO:186) (<u>SEQ ID NO:130</u>)	VGS50-GATTGGCGA CACGGCACCCGTGCC A (SEQ ID NO:187) (<u>SEQ ID NO:168</u>)
2	VGS30-gtagcc gccATGTCACTA CCCAGCTGGCTA ACAGA (SEQ ID NO:188)	VGS31gtaTTAC CGCGGCATCAGC TTGGTGACC (SEQ ID NO:190)	VGS59-GTACGG CGTGCTAATCGT CTTCGGC (SEQ ID NO:191)	VGS60-ATTGCGAGC AGTGCGCATGATGGG C (SEQ ID NO:192)

	DEL1937-gccg ccATGAATCAGA CGGAGCCCGCCC AGC (SEQ ID NO:189)			
3	DEL1840-gccg ccATGTCGGAGA TTGTCGACACCG AGC (SEQ ID NO: 193)	DEL1860-TTCC AGTGGCAGGACA GATCGGGAT (SEQ ID NO:194)	VGS65-ATGTGG CCAGATGGACGA TATCCCA (SEQ ID NO:195)	VGS66-CAATCATGG GAATGCCCCGTAGTCA G (SEQ ID NO:196)
4	DEL1933-gccg ccATGGAGAACA CCACAATGCTGG CTA (SEQ ID NO:197)	DEL1934-TTAG AGTCCAGTGGTG GAGGTCCTG (SEQ ID NO:198)	VGS47-GCCATC ATCCGGCCACTG CAGCCGC (SEQ ID NO: 199)	VGS48-AATGGGATT GTACATGGAGTTGCT C (SEQ ID NO: 200)
5	DEL1844-gccg ccATGGAGAATC GCAGTGACTTCG AGGC (SEQ ID NO:201)	DEL1845-tcta gaTCAGGAGAGC AGTTGGGTGGTG TTGGC (SEQ ID NO:202)	DEL1891-ATCT CCATCGACAGAT ACGT (SEQ ID NO:203)	DEL1892-GCCGCGA TGGCCAGGTTGCA (SEQ ID NO:204)
6	DEL1842-gccg ccATGTACTACA TAGCTCACCAGC AGCCG (SEQ ID NO:205) DEL1990-gccg ccATGGAGCACC ACAATAGCCATC TGTT (SEQ ID NO:206)	DEL1862-CGAT CGGCGCACCGBA GAATCAGTT (SEQ ID NO:207) DEL1989-TCAA AACTCGGTGCTT CTTATGTTTG (SEQ ID NO:208)	VGS51-GTCACC AATTACTTTATA GCCAGCT (SEQ ID NO:209)	VGS52-GGGCAGCCA ACAGCAGGTGAACAC A (SEQ ID NO:210) DEL1991-GTGAGAT GACTACGAAGTACCA TC (SEQ ID NO:211)
7	VGS69-gtagcc gccATGGCAATG GACTTAATCGAG CA (SEQ ID NO:212)	VGS70-TTAAAG TGGTTGCCACAA GGACT (SEQ ID NO:213)	VGS74-GGGCAC ACGTGCTCCTGG TAACG (SEQ ID NO:214)	VGS73-ATAGAGCTG CAGTGGCAGCCAGC (SEQ ID NO:215)
8	VGS38-gtagcc gccATGTTTACG TGGCTGATGATG GATGT (SEQ ID NO: 216)	VGS39-gtaATT ACAAATCTGTCT GCTGCACTGCG (SEQ ID NO:217)	VGS55-GTGCAA AGCCTACATGGT GAGCACA (SEQ ID NO:218)	VGS56-TGAGTATTT CCAGTCGGGAGAGGT C (SEQ ID NO:219)

9	VGS40-gtagcc gccATGTTCAAC TACGAGGAGGGG GATGC (SEQ ID NO:220)	VGS41-gtaTTA GAGCTGAGGACT GTTGACGGCG (SEQ ID NO:221)	VGS53-GTGCTC TGCATGCCCCGTC ACCCTGG (SEQ ID NO:222)	VGS54-GACGAACAG CATCTTGACCACAG C (SEQ ID NO:223)
11	DEL1905-gccg ccATGGCTGGCC ATCAGTCGCTGG CAC (SEQ ID NO:224)	DEL1906-TTAG AGCATTTCAATA TTGGACGTT (SEQ ID NO:225)	VGS57-CCCGTG ACTAGCATGTCC CTGCGAA (SEQ ID NO:226)	VGS58-ACCGGAATC GCAGTCGTCACAATC G (SEQ ID NO:227)

Please replace paragraph [000376] beginning on page 110 with the following amended paragraph:

[000376] A table matching the ligands with their associated receptors is shown below in Table 7.

Table 7

GPCR	SEQ ID NO	Peptide Matching Sequence
dmgpcr1	SEQ ID NO:186	AQRSPSLRLRF-NH ₂
	SEQ ID NO:187	PIRSPSLRLRF-NH ₂
	SEQ ID NO:25	TDVDHVFLRF-NH ₂
	SEQ ID NO:26	DPKQDFMRF-NH ₂
	SEQ ID NO:27	PDNFMRF-NH ₂
	SEQ ID NO:28	TPAEDFMRF-NH ₂
	SEQ ID NO:29	SLKQDFMHF-NH ₂
	SEQ ID NO:30	SVKQDFMHF-NH ₂
	SEQ ID NO:31	AAMDRY-NH ₂
	SEQ ID NO:32	SVQDNFMHF-NH ₂

	SEQ ID NO: 33	ARGPQLRLRF-NH ₂
dmgpcr4	SEQ ID NO: 34	GDGRLYAFGL-NH ₂
	SEQ ID NO: 35	DRLYSFGL-NH ₂
	SEQ ID NO: 36	APSGAQRLYGFGL-NH ₂
	SEQ ID NO: 37	GGSLYSFGL-NH ₂
	SEQ ID NO: 38	FIRF-NH ₂
dmgpcr6 (6a)	SEQ ID NO: 39	KNEFIRF-NH ₂
	SEQ ID NO: 40	FMRF-NH ₂
	SEQ ID NO: 41	KSAFMRF-NH ₂
	SEQ ID NO: 42	KPNFLRF-NH ₂
	SEQ ID NO: 43	FLRF-NH ₂
	SEQ ID NO: 44	YLRF-NH ₂
	SEQ ID NO: 45	KPNFLRY-NH ₂
	SEQ ID NO: 46	TNRNFLRF-NH ₂
	SEQ ID NO: 47	RNKFEFIRF-NH ₂
	SEQ ID NO: 48	AGPRFIRF-NH ₂
	SEQ ID NO: 49	GLGPRPLRF-NH ₂
	SEQ ID NO: 50	IL-Nle-RF-NH ₂
	SEQ ID NO: 51	AGAKFIRF-NH ₂
	SEQ ID NO: 52	APKPKFIRF-NH ₂
	SEQ ID NO: 53	KSAFVLRF-NH ₂

	SEQ ID NO:54	TKFQDFLRF-NH ₂
	SEQ ID NO:55	SAEPFGTMRF-NH ₂
	SEQ ID NO:56	ASEDALFGTMRF-NH ₂
	SEQ ID NO:57	SADDSAPFGTMRF-NH ₂
	SEQ ID NO:58	EDGNAPFGTMRF-NH ₂
	SEQ ID NO:59	FLFQPQRF-NH ₂
dmgpcr6 6aL and 6bL	SEQ ID NO:60	SADPNFLRF-NH ₂
	SEQ ID NO:61	SQPNFLRF-NH ₂
	SEQ ID NO:62	ASGDPNFLRF-NH ₂
	SEQ ID NO:63	SDPNFLRF-NH ₂
	SEQ ID NO:64	AAADPNFLRF-NH ₂
	SEQ ID NO:65	PNFLRF-NH ₂
	SEQ ID NO:66	KPNFLRF-NH ₂
	SEQ ID NO:67	AGSDPNFLRF-NH ₂
	SEQ ID NO:68	KPNFLRY-NH ₂
	SEQ ID NO:69	SPREPIRF-NH ₂
	SEQ ID NO:70	LRGEPIRF-NH ₂
	SEQ ID NO:71	SPLGTMRF-NH ₂
	SEQ ID NO:72	EAEPLGTMRF-NH ₂
	SEQ ID NO:73	ASEDALFGTMRF-NH ₂
	SEQ ID NO:74	EDGNAPFGTMRF-NH ₂

SEQ ID NO: 75	SAEPFGTMRF-NH ₂
SEQ ID NO: 76	SADDAPFGTMRF-NH ₂
SEQ ID NO: 77	KPTFIRF-NH ₂
SEQ ID NO: 78	ASPSFIRF-NH ₂
SEQ ID NO: 79	GAKFIRF-NH ₂
SEQ ID NO: 80	AGAKFIRF-NH ₂
SEQ ID NO: 81	APKPKFIRF-NH ₂
SEQ ID NO: 82	KSAYMRF-NH ₂
SEQ ID NO: 83	SPMQRSSMVRF-NH ₂
SEQ ID NO: 84	SPMERSAMVRF-NH ₂
SEQ ID NO: 85	SPMDRSKMVRF-NH ₂
SEQ ID NO: 86	KNEFIRF-NH ₂
SEQ ID NO: 87	KPSFVRF-NH ₂
SEQ ID NO: 88	pQPKARSGYIRF-NH ₂
SEQ ID NO: 89	AMRNALVRF-NH ₂
SEQ ID NO: 90	ASGGMRNALVRF-NH ₂
SEQ ID NO: 91	NGAPQPFVRF-NH ₂
SEQ ID NO: 92	RNKFEFIRF-NH ₂
SEQ ID NO: 93	SDRPTRAMDSPLIRF-NH ₂
SEQ ID NO: 94	AADGAPLIRF-NH ₂
SEQ ID NO: 95	APEASPFIRF-NH ₂

SEQ ID NO:96	ASPSAPLIRF-NH ₂
SEQ ID NO:97	SPSAVPLIRF-NH ₂
SEQ ID NO:98	ASSAPLIRF-NH ₂
SEQ ID NO:99	KHEYLRF-NH ₂
SEQ ID NO:100	SLLDYRF-NH ₂
SEQ ID NO:101	EIVFHQISPIFFRF-NH ₂
SEQ ID NO:102	GGPQGPLRF-NH ₂
SEQ ID NO:103	GPSGPLRF-NH ₂
SEQ ID NO:104	AQTFVRF-NH ₂
SEQ ID NO:105	GQTFVRF-NH ₂
SEQ ID NO:106	KSAFVRF-NH ₂
SEQ ID NO:107	KSQYIRF-NH ₂
SEQ ID NO:108	DVPGVLRf-NH ₂
SEQ ID NO:109	KSVPGVLRf-NH ₂
SEQ ID NO:110	SEVPGVLRf-NH ₂
SEQ ID NO:111	SVPGVLRf-NH ₂
SEQ ID NO:112	DFDGAMPGVLRf-NH ₂
SEQ ID NO:113	EIPGVLRf-NH ₂
SEQ ID NO:114	WANQVRF-NH ₂
SEQ ID NO:115	ASWASSVRF-NH ₂
SEQ ID NO:116	AMMRF-NH ₂

SEQ ID NO:117	GLGPRPLRF-NH ₂
SEQ ID NO:118	SPSAKWMRF-NH ₂
SEQ ID NO:119	TKFQDFLRF-NH ₂
SEQ ID NO:120	pQDRDYRPLQF-NH ₂
SEQ ID NO:121	FIRF-NH ₂
SEQ ID NO:122	AVPGVLRf-NH ₂
SEQ ID NO:123	GDVPGVLRf-NH ₂
SEQ ID NO:124	SDIGISEPNFLRF-NH ₂
SEQ ID NO:125	SGKPTFIRf-NH ₂
SEQ ID NO:126	AEGLSSPLIRf-NH ₂
SEQ ID NO:127	FDRDFMRF-NH ₂
SEQ ID NO:128	AGPRFIRf-NH ₂
SEQ ID NO:129	GMPGVLRf-NH ₂
SEQ ID NO:130	IL-Nle-Rf-NH ₂
SEQ ID NO:131	LQPNFLRF-NH ₂
SEQ ID NO:132	KPNFIRf-NH ₂
SEQ ID NO:133	FMRF-NH ₂
SEQ ID NO:134	FLRF-NH ₂
SEQ ID NO:135	YIRf-NH ₂
SEQ ID NO:136	GNSFLRF-NH ₂
SEQ ID NO:137	DPSFLRF-NH ₂

	SEQ ID NO:138	pQDFMRF-NH ₂
	SEQ ID NO:139	KPNQDFMRF-NH ₂
	SEQ ID NO:140	TDVDHVFLRF-NH ₂
	SEQ ID NO:141	AAMDRY-NH ₂
	SEQ ID NO:142	SPKQDFMRF-NH ₂
	SEQ ID NO:143	PDNFMRF-NH ₂
	SEQ ID NO:144	DPKQDFMRF-NH ₂
	SEQ ID NO:145	TPAEDFMRF-NH ₂
	SEQ ID NO:146	SDNFMRF-NH ₂
	SEQ ID NO:147	YLRF-NH ₂
	SEQ ID NO:148	SDRNFLRF-NH ₂
	SEQ ID NO:149	TNRNFLRF-NH ₂
	SEQ ID NO:150	PDVDHVFLRF-NH ₂
	SEQ ID NO:151	pQDVDHVFLRF-NH ₂
	SEQ ID NO:152	FLFQPQRF-NH ₂
	SEQ ID NO:153	ARGPQLRLRF-NH ₂
	SEQ ID NO:154	FDDY (SO ₃ H) GHLRF-NH ₂
	SEQ ID NO:155	FDDYGHLRF-NH ₂
	SEQ ID NO:156	MDSNFIRF-NH ₂
dmgpcr9	SEQ ID NO:157	FDDY (SO ₃ H) GHLRF-NH ₂
dmgpcr5	SEQ ID NO:169	APTSSFIGMR-NH ₂

	SEQ ID NO:170	APLAFYGMN-NH ₂
	SEQ ID NO:171	APLAFYGLR-NH ₂
	SEQ ID NO:172	APTGFTGMN-NH ₂
	SEQ ID NO:173	APVNSFVGMN-NH ₂
	SEQ ID NO:174	APNGFLGMN-NH ₂
dmgpcr7	SEQ ID NO:175	DPAFNWSG-NH ₂
	SEQ ID NO:176	GSGFSSWG-NH ₂
	SEQ ID NO:177	pGlu-SSFHWSG-NH ₂
	SEQ ID NO:178 SEQ ID NO:231	GASFYSWG-NH ₂
	SEQ ID NO:179	NPFHWSG-NH ₂
	SEQ ID NO: 180	PSFHWS-NH ₂
	SEQ ID NO: 181	NSVVLGKKQRFHWSG-NH ₂
	SEQ ID NO:182	pGlu-RFHWSG-NH ₂
	SEQ ID NO: 183	QRFHWSG-NH ₂
dmgpcr8	SEQ ID NO:184	pGlu-VRFRQCYFNPISCF-OH _____
	SEQ ID NO:185	pGlu-VRFRQCYFNPISCF-OH _____